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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/687,951	10/13/00	CLELAND J	M-9177-US

EXAMINER	
KAM, C	
ART UNIT	**PAPER NUMBER**
1653	2

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DATE MAILED: 01/18/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

PTO-90C (Rev. 2/95)

U.S. G.P.O. 1999 460-693

1- File Copy

Office Action Summary	Application No.	Applicant(s)	
	09/687,951	CLELAND ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15)☒ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 1-3 are rejected as being indefinite because claims 1 recites the limitation "the concentration of about 0.01 to about 0.8 percent by volume" in line 2 of the claim. There is insufficient antecedent basis for this limitation in the claim. The specification discloses the preferred range of the concentration for hyaluronic acid is between 0.01 percent to 0.8 percent (w/v, see page 8, line 2-5) and % by volume is not weight per volume.

2. Claims 1, 3-5, 17, 18 and 20 are rejected as being indefinite because of the use of the term "a derivative thereof". The term "a derivative thereof" renders the claim indefinite, it is unclear in the claim what kind of derivative of hyaluronic acid is intended.

3. Claims 4, 5, 15, 16 and the claims dependent these to are indefinite as to what the "effective amount of the biologically active agent" is supposed to do.

4. Claim 9 is rejected as being indefinite because of the use of the term "a mixture of biodegradable and non-biodegradable polymers, and a copolymer comprising biodegradable and non-biodegradable units ". Note that Markush groups must be closed and "a mixture of.... and a copolymer ....." is open language in regard to the amounts of each in the mixture and in the copolymer which are unrecited and make the mixture undefined.

5. Claim 10 is rejected as being indefinite because of the use of the term "and mixtures thereof". Note that Markush groups must be closed and "and mixtures thereof" is open language in regard to the number of components and amounts of each in the mixtures which are defined.

6. Claim11 is rejected as being indefinite because of the use of the term "and a blend or copolymer thereof". Note that Markush groups must be closed and "and a blend or copolymer thereof" is open language in regard to the number of components and amounts of each in the blend or copolymer which are undefined in the claim.

7. Claims 7, 15 and 16 are rejected as being indefinite, because neither the claim nor the specification define the term "between about....about..." for the concentration of hyaluronic acid. The term "between about....about..." renders the claim indefinite, it is unclear what the range of the concentration is. Deletion of "between" or "about" (both instances) is suggested.

8. Claims 15 and 16 are rejected as being indefinite, because neither the claim nor the specification define the term "at least about" for the concentration of hyaluronic acid. The term "at least about" renders the claim indefinite, it is unclear what the concentration of hyaluronic acid is. Deletion of "at least" or "about" is suggested.

9. Claims 18-19 are rejected as being indefinite because they lack essential steps cited in the process of producing a pharmaceutical formulation. The omitted steps are the analysis and evaluation of the pharmaceutical formulation.

10. Claim 20 is rejected as being indefinite because they lack essential steps cited in the process of administering a pharmaceutical formulation by injection. The omitted steps are the sites of administration and the evaluation for injection of the pharmaceutical formulation.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-6, 8-11, 13-14 and 17-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Igari *et al.* (US 5,416,071).

Igari *et al.* teach a water soluble composition containing a pharmacologically active polypeptide and hyaluronic acid or its nontoxic salts which can be administered to patients by injection (columns 3, 4, 6-10, 12, 13, 15 and Examples). The liquid form or the lyophilized powder form of this composition is dispersible in a solution of biodegradable polymer such as poly(lactic-glycolic)acid copolymer (column 15, lines 35-54).

12. Claims 1-13, and 15-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Machida *et al.* (EP 0,263,490).

Machida *et al.* teach a sustained-release particulate preparation containing a polymer, a pharmacologically active agent and a natural high molecular weight of sugar such as hyaluronic acid as well as a process of preparing the preparation. The preparation is administered subcutaneously or intramuscularly for obtaining a long-lasting pharmacological activity (columns 3, 4 and Example 1 and 3).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 1-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Igari *et al.* (US 5,416,071) taken with Machida *et al.* (EPA 0 263 490).

Igari *et al.* disclosed preparations (abstract) containing hyaluronic acid and a biological agent (abstract and at least col. 9-16 as well as the examples) delivered by injection (abstract, col. 8-9, note the 26G needle (col. 4, lines 10+)) in final concentrations of 0.02 to less than 1%

(col. 7, lines 50+ and col. 13, lines 42+) dissolved in, e.g., physiological saline (col. 8, lines 60+) which are anticipatory of claims 1-3. Formulations as microcapsules or nanospheres is also disclosed (col. 15, lines 35+) and would have been expected to contain, e.g., poly(lactic-glycolic) acid copolymers. The foregoing are applicable to claims 1-14 and 17-20 as anticipatory but where the Igari *et al.* reference does not appear to disclose the amount of the polymeric matrix in the formulation, it would nevertheless have been obvious to one of ordinary skill in the art from the teaching in Igari *et al.* reference to have made particulate formulations for the reasons indicated above and for slow/timed release of the biologically active agent. Thus, one of ordinary skill in the art would have combined the Igari *et al.* teachings with that of the Machida *et al.* reference to obtain the sustained release particulate preparations (abstract) for long lasting pharmacological action. Machida *et al.* like Igari *et al.* teach various proteins (e.g., col. 3-4), use of hyaluronic acid (col. 3) and that the amount of the matrix is 0.1 to 20% by weight or 1 to 20-fold by volume which, absent teaching to the contrary, appears to meet the criteria for claims 15 and 16. As stated, the combined references result in all aspects of the claimed subject matter which shows that the claimed invention was within the ordinary skill in the art to make and use at the time it was made and was as a whole, *prima facie* obvious.

Conclusion

14. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D.

Patent Examiner

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January 15, 2001

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